

NIAMS IRPartners

Spring/Summer 2009

A newsletter for
patients of the Intramural
Research Program (IRP),
National Institute
of Arthritis and
Musculoskeletal and
Skin Diseases (NIAMS)

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For a Future Clinician Scientist, Success Is a Journey

Adewole Adamson, who goes by Ade, is a fellow working in the NIAMS Intramural Research Program. He began his fellowship in August 2008 as part of the Clinical Research Training Program, a 12-month program designed to attract the most creative, research-oriented medical and dental students to the intramural campus of NIH. Ade is currently conducting basic scientific research related to immunology and will complete his work with NIAMS this summer.



Adewole Adamson

Ade has a unique culturally diverse background and is proficient in three languages, having been raised in four countries: the United States, Canada, Somalia, and Guatemala. Despite his global experiences, Ade often considered himself an outsider while growing up.

"I traveled a lot, so I experienced some problems relating to people," says Ade. "When I resided in Canada, I was the only African American non-French speaker in my school." However, he immediately learned that science was one language that was universal. "I found ways to be involved. It became evident to my understanding that science connected people across cultures." Although his father is a physician, Ade was never predisposed to scientific research. "My dad was a doctor, but when he came home from work, he was just my dad. I never talked to him about medicine until medical school."

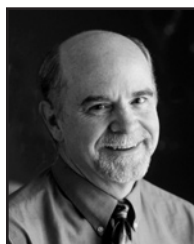
His exposure to research in high school initiated his appreciation for science. "My interest in science was given a deeper meaning my junior year of high school when I participated in the Gene Search Program at Catholic University of America, a program funded by NIH," shares Ade. In the summer of his senior year in high school, Ade was working at a department store when he received a phone call from his high school chemistry professor informing him that he was invited to continue his work in the Gene Search Program, which exposed him to scientific research techniques such as electrophoresis, polymerase chain reaction (PCR), cell culturing, enzyme-linked immunosorbent assay (ELISA), and bacteria transformation. This meaningful experience contributed to his aspiration of pursuing a career in science.

From the Scientific and Clinical Directors

It has been a busy several months for the NIAMS Intramural Research Program since our last issue of *IRPartners*.

This issue contains a story about a NIAMS fellow whose talents and heritage make him a unique asset to the Institute. Then, we pay a visit to the NIH Pediatric Rheumatology Clinic, which offers diagnosis, evaluation, and treatment for children with arthritis and other chronic rheumatic diseases who are enrolled in clinical trials.

*John O'Shea, M.D.
Scientific Director
Intramural Research Program
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National Institutes of Health*



In addition, we welcome new staff members to NIAMS and celebrate the accomplishments of several others. We also provide a synopsis of recent intramural research highlights.

Lastly, our "HPP Spotlight" features La Clínica del Pueblo, located in the Columbia Heights neighborhood of Washington, DC.

We hope you enjoy this issue, and we look forward to sharing future highlights and advances with you.

*Daniel Kastner, M.D., Ph.D.
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Pediatric Rheumatology Clinic Combines Comprehensive Mission With Single Purpose

In the fall of 2000, NIH established its first Pediatric Rheumatology Clinic with the aim of achieving a broad and vitally important mission. The clinic provides assessment, diagnosis, and treatment for children enrolled in an NIH study who are diagnosed with or suspected of having a rheumatic condition. It also serves as a health education center, providing evidence-based information on the signs and symptoms of rheumatic diseases along with tips for managing these conditions. For physicians, the clinic offers exposure to and training in the subspecialty of pediatric rheumatology. Finally, by enrolling patients in ongoing clinical trials, the clinic contributes to the understanding of the causes of rheumatic diseases in young people.

In addition to this comprehensive focus, the clinic covers a diverse set of interrelated conditions. The clinic is open to patients dealing with any of more than 100 rheumatic diseases, which are defined as those involving inflammation of muscles, joints, tendons, ligaments, bones, and skin, as well as to young people who have received diagnoses for multiple conditions. Currently, the clinic has studies under way on juvenile idiopathic arthritis, juvenile



The Pediatric Rheumatology Clinic is located in the NIH Clinical Center.

systemic lupus erythematosus, and periodic fever syndromes, including neonatal onset multisystem inflammatory disease (NOMID).

The symptoms and progression of rheumatic diseases are often markedly different in children than in adults, presenting challenges to the diagnosis and management of these chronic conditions. To meet the medical needs of young patients and support a robust portfolio of research studies, the clinic employs a wide range of health professionals

Ade displays tremendous enthusiasm for the process of scientific investigation and its applications for improving patient care. Since college, he has managed both clinical and research interests. Over the past 5 years, Ade has worked directly with dedicated and gifted researchers at the Jackson Laboratory, Rockefeller University, Morehouse School of Medicine, Harvard Medical School, and Massachusetts Institute of Technology (MIT). Developing a relationship with senior researchers was essential in shaping his concept of a “physician scientist.” Moreover, these experiences have improved his critical thinking skills and scientific techniques and have heightened his knowledge of the process of scientific discovery.

In 2005, Ade graduated from Morehouse College in Atlanta with a double degree in biology and French. He is currently enrolled in the Health Sciences and Technology (HST) program at Harvard Medical School (HMS), a collective research-oriented M.D. program associated with MIT. This unique graduate program allows students in the areas of medicine, engineering, science, and management to train side by side and is especially suited to medical students pursuing research careers in academic medicine.

Throughout his career, Ade has been the recipient of several remarkable awards. In March 2005, he earned the Acres of Diamonds Award for distinction in a national oral presentation and poster session held at NIH as part of the Minority Trainee Research Forum. Likewise, in 2006, Ade was awarded the Louis W. Gilbert Fellowship, funding his thesis in the HST program. He presented his research at the HMS annual research day. Most recently, Ade was selected as a Zuckerman Fellow at Harvard’s John F. Kennedy School of Government. This prestigious fellowship is awarded to 25 students who are pursuing an M.D., J.D., or M.B.A. degree and have a commitment to leadership and public service.

While in medical school, Ade is working at the NIAMS Clinical Research Training Program with John O’Shea, M.D., Scientific Director for the Institute’s Intramural Research Program. Ade is studying Th17 cells, a subset of CD4⁺ T cells, which play an important role in the immune system and have been linked to autoimmune disease. Overactive CD4⁺ T cells can indicate signs of autoimmune disease, whereas low counts of CD4⁺ T cells can indicate signs of immune deficiency diseases such as AIDS. By studying how these cells function in mouse models of autoimmune diseases and in skin



NIAMS fellow Adewole Adamson

samples from human psoriasis disease, Ade can gain a greater understanding of how the cells contribute to autoimmune diseases and, ultimately, how to treat these diseases more effectively. He is very optimistic about his work with NIAMS. “I hope my research will ultimately contribute to helping those who suffer from autoimmune diseases like psoriasis and lupus.”

Despite his hectic schedule, Ade is extremely active in the local community. He serves as head coach for a youth ice hockey team in Maryland, a role that suits him well after playing years of organized ice hockey in Montreal, Canada. In addition, he volunteers as a guest speaker at several public schools in Washington, DC, imparting his knowledge and enthusiasm for his career path to students and addressing issues associated with collegiate life, the process of applying for higher-level education, and the advantages of pursuing a career in science and medicine.

Undeterred by the perpetual demands of a profession in science and medicine, Ade maintains a positive outlook that he would like to impart to youth interested in pursuing a career in science. He shares, “A career in science takes years of practice and devotion. Even though it can be difficult, it is a deeply rewarding career because the discoveries made in the laboratory ultimately change how medicine is practiced, improving the lives of millions.”

Upon completing his research training at NIAMS in August 2009, Ade will obtain his medical degree from Harvard and plans to specialize in immunology and dermatology. He also plans to finish his master’s degree in public policy from Harvard’s Kennedy School of Government. His career goal is to work as a physician scientist for a medical institute similar to NIH. Ade explains, “I would like to become a physician scientist and serve as a link between basic research and applied medicine in the hospital. Ultimately, I would like to be in a position that allows me to impart on future doctors the importance of melding compassionate patient care with the sound knowledge of scientific investigation.” ▲

in addition to pediatric rheumatology fellows, including nurse practitioners, pediatricians, and research nurses. These staff members work closely with referring physicians to inform them about treatments being provided at NIH and to ensure continuity of care when patients return home. The clinic's staff also relies on the expertise available through other components of the NIH Clinical Center, sending patients to the Department of Radiology and Imaging Sciences to assess joint damage and visualize inflammation, or to the Department of Rehabilitation Medicine to improve mobility and restore muscle strength, when necessary.

Although the focus of the Pediatric Rheumatology Clinic is broad, the diseases it addresses are varied, and the services it provides are diverse, the clinic has a unified purpose: improving the lives of children living with rheumatic diseases. In addition to the small group of young people who receive direct care, the research being conducted at the clinic may lead to better diagnostic tools and more effective interventions and, eventually, to reducing the number of children and families affected by pediatric rheumatic diseases.

For more information, call the NIAMS Information Clearinghouse at 301-495-4484 (direct) or 877-22-NIAMS (226-4267) (free of charge).

To find out if a child is eligible for a clinical study, call the NIH Patient Recruitment Office at 800-411-1222 (TTY 866-411-1010). ▲

NIAMS Student Wins Gold at Biology Olympiad



Jonathan Liang

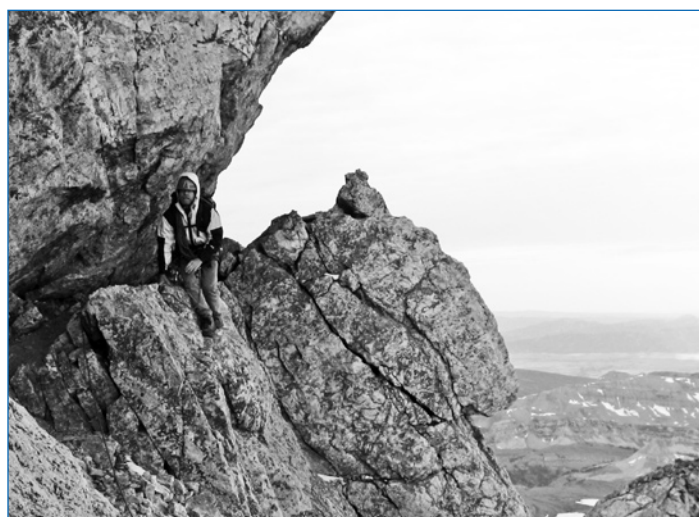
Jonathan Liang, a student at Thomas S. Wootton High School in Rockville and an intern in the NIAMS Molecular Immunology and Inflammation Branch, was awarded a gold medal in the 19th International Biology Olympiad held in Mumbai, India, in 2008. In his role at NIAMS, Jonathan assists researchers who look

at the role that epigenetic modification plays in helper T cell functions. Epigenetic modification is

heritable changes in a cell that are influenced by the environment but are not contained in the sequence of the DNA.

Most student interns come for the summer only, but Jonathan continued working in the NIAMS lab for the entire school year. In the fall, he'll continue on to college, and after he completes his undergraduate work, he plans either to attend medical school or to pursue a Ph.D. Says Jonathan, "Science is more interesting than [a lot of people] think. The opportunity to improve the quality of life for people living with diseases is something that I really want to be a part of." ▲

From Molecules to Mountains: NIAMS' Watts Climbs Alaska's Denali



NIAMS scientist and veteran mountaineer, Norman Watts

NIAMS' Norman Watts, Ph.D., recently returned from his third expedition to the most renowned peak in Alaska (and North America) – Denali. He has been mountaineering for nearly 20 years and has climbed summits up to 23,000 feet. And Dr. Watts knows mountains with fierce and gorgeous names: Condoriri, Baruntse, Denali. "Denali is the native name for Mount McKinley," he says. "It's a serious mountain. You can make arguments that it's the greatest." During his most recent expedition to Denali, Dr. Watts experienced high-altitude cerebral edema and, although he didn't know it at the time, was seriously affected by Lyme disease. Unfortunately, the double whammy forced him back down the mountain.

Dr. Watts works with hepatitis and HIV proteins in two NIAMS labs, the Protein Expression Laboratory with Paul Wingfield, Ph.D., and the Laboratory of Structural Biology Research with Alasdair Steven, Ph.D.

"I've always been a pretty academic person," Dr. Watts says, "but I really love nature. So I get to do two exotic things: electron microscopy and mountaineering. There's no way you can go out there and not be significantly affected. There are reasons people have thought of mountains as deities, as the axis of the Earth." ▲

NIAMS Intern Wins Honor



Alex Matsche with NIAMS' Sharon Louis

Alex Matsche, a former biomedical research intern in the Cartilage Biology and Orthopaedics Branch, NIAMS, was selected for the 2008 Workforce Recruitment Program (WRP) Outstanding Student Award.

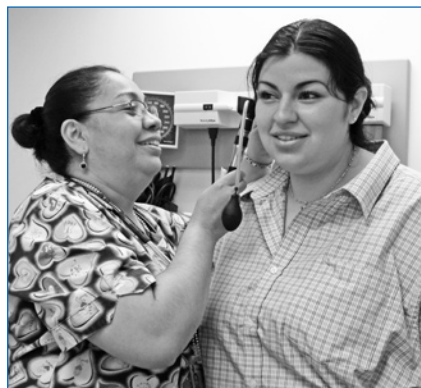
Alex was one of two students selected to receive the award from more than 450 students hired through the program. He was the only winner from the Department of Health and Human Services.

The Department of Labor's Office of Disability Employment Policy and the Department of Defense coordinate WRP, which connects Federal and private-sector employers with highly motivated postsecondary students with disabilities.

Alex analyzed the roles of two cell signaling pathways in mesenchymal stem cells derived from adult human bone marrow during cartilage differentiation. A graduate of Gallaudet University,

Alex will complete his work as an intern at NIAMS and then plans to attend Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California, San Diego, to get his doctor of pharmacy degree. Ultimately, he would like to be involved in the development of new drugs, either by returning to NIH or by working for a drug company. ▲

NIAMS HPP Spotlight: *La Clínica del Pueblo*



When visiting the state-of-the-art facilities of La Clínica del Pueblo in the Columbia Heights neighborhood of Washington, DC, you may not realize that a single

volunteer doctor from El Salvador started all of this in a borrowed room. Twenty-five years later, La Clínica remains true to the mission of Juan Romagoza, M.D., to offer culturally appropriate health services to Hispanics, regardless of their ability to pay, by providing 55,000 client visits per year to a patient population that is 90 percent uninsured. The bilingual staff at La Clínica supports a vast array of programs, including mental health, substance abuse, HIV/AIDS, and social services.

The services of La Clínica reach well beyond its doors. Its Interpreters Program serves patients with limited English proficiency at medical facilities throughout the Washington metropolitan area and recently secured an important contract with the District of Columbia to provide medical interpretation training to hundreds of people in the city. La Clínica also holds dozens of outreach events and health fairs annually. Through its Health Partnership Program (HPP), NIAMS provides printed materials and experts on lupus, arthritis, and other rheumatic diseases at some of the venues to support this educational effort.

La Clínica is located at 831 15th Street, N.W., Washington, DC 20009-4607. To learn more about this valuable HPP partner, visit its Web page at www.lcdp.org. ▲

Immune System Flexibility Identified in Helper T Cell Function

In collaboration with researchers at the National Institute of Allergy and Infectious Diseases and the National Heart, Lung, and Blood Institute, NIAMS Scientific Director John J. O'Shea, M.D., and his colleagues have discovered a new explanation for the flexibility of responses of one type of immune system cell, called T lymphocytes, using a new genome sequencing technology that surveys the cells' epigenomes. The epigenome is the heritable cellular information, other than DNA, that affects phenotype. Their work, which has generated the largest blueprint of its kind for studying the biology of these cells, provides new clues about the epigenetic regulation of key immune genes – clues that could one day be used to treat diseases, particularly autoimmune and infectious diseases. Their findings were reported in the journal *Immunity*.

Wei G, Wei L, Zhu J, et al. Global Mapping of H3K4me3 and H3K27me3 reveals specificity and plasticity in lineage fate determination of differentiating CD4⁺ T cells. *Immunity*. 2009;30(1):155-167.

A Key to Understanding Lymphoma

Rafael Casellas, Ph.D., and his team in the Genomics and Immunity Group within the Molecular Immunology and Inflammation Branch of NIAMS, along with researchers from the National Cancer Institute, looked into the role of a certain kind of white blood cell, known as a B cell, in the origin of lymphoma. Existing research has shown that more than 95 percent of all lymphomas diagnosed in the Western World are of B cell origin. In recent years, an enzyme in B cells called activation-induced cytidine deaminase (AID) has been linked to the formation of tumors. Dr. Casellas and his colleagues demonstrated that the incidence of lymphoma tumors is directly proportional to the amount of AID in the B cell. This research suggests that AID can be targeted for future therapies to fight lymphoma and to alleviate the suffering it causes. These findings were recently published in the *Journal of Experimental Medicine*.

Takizawa M, Tolarová H, Li Z, et al. AID expression levels determine the extent of *cMyc* oncogenic translocations and the incidence of B cell tumor development. *Journal of Experimental Medicine*. 2008;205(9):1949-1957. Epub 2008 Aug 4. PMID: 18678733.

Communication Between Immune Cells Can Dampen Allergic Reactions

Juan Rivera, Ph.D., Acting Chief of the NIAMS Laboratory of Immune Cell Signaling, in collaboration with researchers in Italy, has found that communication between two immune system cells can decrease allergic responses in mice. The study appeared in a recent issue of the journal *Immunity*. Rivera and his colleagues studied two seemingly unconnected immune system cells: T regulatory cells (Tregs) and mast cells. They showed that direct interaction between the two cells, in the form of cell surface to cell surface binding, suppressed the release of inflammatory factors from mast cells. Until this study, researchers were unaware of this mechanism for regulating allergic reactions. The researchers then studied mice with inactive Treg cells and found that they had increased allergic responses. In addition, the researchers removed the binding sites from the Tregs and mast cells in other mice and found that these mice also had increased allergic responses. These findings may lead to a better understanding of why some people are more predisposed to allergic reactions and possibly contribute to the development of therapies to counteract or prevent these conditions.

Gri G, Piconese S, Frossi B, et al. CD4⁺CD25⁺ regulatory T cells suppress mast cell degranulation and allergic responses through OX40-OX40L interaction. *Immunity*. 2008;29(5):771-781.

NIAMS Scientists Discover a New Source of Progenitor Cells in Traumatized Tissue

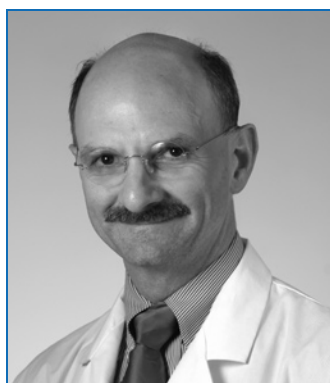
Researchers in the Cartilage Biology and Orthopaedics Branch of NIAMS, in collaboration with orthopaedic surgeons at the Walter Reed Army Medical Center, have discovered that tissue removed

from traumatic wounds, traditionally considered medical waste, can be a source of progenitor cells. The findings were recently published in two research reports in the *Journal of Bone and Joint Surgery* and the *Journal of Tissue Engineering and Regenerative Medicine*. Progenitor cells feature many of the same properties as adult stem cells, particularly in that they have the capacity to differentiate into multiple cell types. Researchers are currently studying ways to use progenitor cells to improve healing at the site of an injury, and traumatized tissue may provide an alternative source of cells for these therapies.

Nesti LJ, Jackson WM, Shanti RM, et al. Differentiation potential of multipotent progenitor cells derived from war-traumatized muscle tissue. *Journal of Bone and Joint Surgery*. American volume. 2008;90(11):2390-2398.

Jackson WM, Aragon AB, Djouad F, et al. Mesenchymal progenitor cells derived from traumatized human muscle. *Journal of Tissue Engineering and Regenerative Medicine*. 2009; 3(2):129-138. ▲

Colbert Named NIAMS Pediatric Branch Chief



Robert A. Colbert, M.D., Ph.D., has been named Chief of the Pediatric Translational Research Branch in NIAMS' Intramural Research Program. He most recently served as Director of the Division of Rheumatology at

Cincinnati Children's Hospital Medical Center of the University of Cincinnati College of Medicine, with which he has been affiliated since 1994, when he joined the Department of Pediatrics.

Dr. Colbert earned his bachelor's degree in chemistry and biology from Boston University in 1978 and his M.S. in biochemistry from the University of Vermont in 1980. In 1986, he received his Ph.D. in biophysics from the University of Rochester School of Medicine; the following year he received his M.D. from the same institution. Rochester was also the place where he served his internship and residency in pediatrics, at the university's Strong Memorial Hospital.

Dr. Colbert then completed a clinical fellowship in pediatric rheumatology at Duke University Medical Center and North Carolina Memorial Hospital of the University of North Carolina (UNC). He finished his postdoctoral research training in the Department of Microbiology and Immunology at UNC.

Dr. Colbert is certified in pediatric rheumatology by the American Board of Pediatrics and is a member of several organizations, including the American

Academy of Pediatrics, the American Association of Immunologists, and the American Pediatric Society. He has authored 53 papers and has served as an investigator on a number of research studies funded by NIAMS, other NIH Institutes, and industry. He has received numerous honors and awards, including Pfizer Postdoctoral Fellowship and Scholar Awards, the James R. Klinenberg Science Award from the Arthritis Foundation, and, more recently, recognition by the American College of Rheumatology with the Deborah Kredich Pediatric Rheumatology Service Award. ▲



Need an NIH Speaker?

The NIH Speakers Bureau is a service that lists NIH researchers, clinicians, and other professionals who are available to speak to school groups and other

local and national organizations. Speakers have expertise in such areas as arthritis, osteoporosis, autoimmunity, and several dozen other topics covered by NIH. To find out more about this service, sponsored by NIH's Office of Science Education, visit its Web site at <http://science.education.nih.gov/spkbureau.nsf>.

Bhattacharyya Joins NIAMS Orthopaedic Research Program



Augmenting NIAMS' efforts in the area of outcomes research, Timothy Bhattacharyya, M.D., has joined the Clinical and Investigative Orthopaedics Section of the Intramural Research Program. A staff orthopaedic surgeon at Bethesda's Suburban Hospital since 2008,

Dr. Bhattacharyya will continue seeing patients and conducting surgery at that facility while working part-time for NIAMS.

Dr. Bhattacharyya received his undergraduate education at Northwestern University in Evanston, IL, from which he graduated with distinction in 1994. He received his medical degree from Washington University in St. Louis in 1998, which he followed with an internship in general surgery and a residency in orthopaedic surgery, both at the Boston University/Boston Medical Center. Following the completion of his residency in 2003, Dr. Bhattacharyya entered a yearlong fellowship in orthopaedic trauma at Harvard Medical School. From 2004 to 2008, he served on the school's faculty as an instructor of orthopaedic surgery while working as a staff orthopaedic surgeon at both Massachusetts General Hospital and Brigham and Women's Hospital. His efforts as an instructor were honored in 2008 with the "Golden Apple" – Harvard's Combined Orthopaedic Residency Program Teacher of the Year Award.

A member of the American Academy of Orthopaedic Surgeons, the Orthopaedic Trauma Association, and the Massachusetts Medical Society, Dr. Bhattacharyya currently serves on the Health Care System Committee of the American Academy of Orthopaedic Surgeons. While at Massachusetts General, he was appointed to the hospital's Clinical Research Council and the Department of Orthopaedic Surgery's Quality Assurance Committee.

As a researcher, Dr. Bhattacharyya covers a wide range of issues, including surgical interventions following orthopaedic trauma, the medical and legal aspects of orthopaedic care, and the impact of

pay-for-performance measures. He has authored or coauthored more than 25 publications and has made numerous presentations in forums such as the annual meetings of the American Orthopaedic Association and the Orthopaedic Trauma Association. He also serves as a reviewer for the journals *Clinical Orthopaedics and Related Research* and the *Journal of Bone and Joint Surgery*. ▲

Questions to Consider Before Joining a Study

- What is the purpose of the study?
- What is required of me?
- Will the study benefit me or others?
- Are there risks? If so, what are they and what are the chances that they will occur?
- What discomforts are involved?
- How long will the study last?
- What will happen if I decide to leave the study?

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